Endovascular repair of mycotic aortic aneurysms

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Purpose: **We report our single-center experience of early and midterm outcome after endovascular repair of mycotic aortic aneurysms (MAA).**
Methods: **Case records were retrospectively reviewed of 11 patients who underwent endovascular repair of 13 MAAs between 2000 and 2007. The aneurysms were localized in the aortic arch in 1 patient, descending thoracic aorta in 4, suprarenal abdominal aorta in 3, and infrarenal abdominal aorta in 5.**
Results: **Mean follow-up was 27 months. A bleeding aortoesophageal fistula resulted in one in-hospital death ≤30 days. Three patients died later: one each of sepsis, stent migration that caused intestinal ischemia, and an unknown cause. Two patients had recurrent sepsis postoperatively but no vascular complications, two had elevated inflammatory markers during follow-up but were asymptomatic, and three patients had an uneventful follow-up.**
Conclusions: **Endovascular treatment for MAA was feasible, with acceptable perioperative mortality and midterm outcome in this single-center case series. Recurrent sepsis and late relapse with a second MAA occurred, indicating the need of long-term antibiotic therapy and follow-up, as well as the possible need for secondary open repair in selected cases. Further research is warranted to evaluate long-term outcome. (J Vasc Surg 2009;50:269-74.)**

Mycotic aortic aneurysm (MAA) is a rare but life-threatening disease, with an incidence of about 0.65% to 2% of all aortic aneurysms.[1,2] The disease has a very poor prognosis for several reasons: MAAs have an increased tendency to grow rapidly and to rupture,[3] and patients with MAA often have severe comorbidities (eg, immunosuppression) and coexisting sepsis.[4] Conventional surgical treatment, which consists of a radical operation with resection of the aneurysm, extensive local débridement, and revascularization by in situ reconstruction or extra-anatomic bypass is the gold standard but carries a high mortality. Open surgery is also associated with morbidity and risk for fatal late complications, in particular, aortic stump blow-out.[5] Furthermore, a more variable and precarious location of the aneurysms sometimes makes surgical repair very demanding or even impossible.[6]

Endovascular aneurysm repair (EVAR) is a less invasive but controversial alternative to conventional open repair of MAA. A major disadvantage is that the infected tissue, including the aneurysm itself, is not resected, which may facilitate reinfection, recurrent sepsis, and infection of the endoprosthesis. Another drawback is that representative microbiologic cultures from the infected tissue are not harvested, making the diagnosis more dubious and the postoperative antibiotic strategy less precise. However, a less invasive treatment may reduce early operative mortality and morbidity, especially in high-surgical-risk patients. The effect on late complications may also differ. EVAR for MAA may be considered a permanent treatment or a bridge to open surgery, allowing the patient to recover from the state of emergency and sepsis, to be more permanently treated later on with elective open repair.

Earlier reports on EVAR for MAA have shown promising results; however, only a few case reports and small series[7] with limited follow-up have been published. The crucial question of durability therefore remains unanswered. The aim of this single-center study was to analyze early and midterm outcome of endovascularly treated MAA.

METHODS

All patients treated for MAA at Uppsala University Hospital between January 2000 and December 2007 were identified by scrutinizing four different data sources: The Swedvasc registry, the registry of the Radiological Department, the In-Patient Registry of the University Hospital, and a specific list updated continuously by the investigators. Case records were reviewed retrospectively. Patient characteristics (sex, age, medical history, symptoms, concurrent infection, and results of microbiologic cultures), aneurysm characteristics, treatment method, early and late complications, and survival were evaluated. The diagnosis of MAA was based on a combination of clinical presentation, results of hematologic tests and cultures, and radiologic findings on computed tomography (CT), for example, saccular multilobular aneurysms or eccentric aneurysms with narrow neck, rapid expansion, periaortic gas formation within the aneurysm thrombus, and periaortic soft tissue mass.[8]

Patients were reassessed postoperatively with a clinical examination, hematologic tests, and imaging at 1, 6, and 12 months, and then annually thereafter. If a complication was suspected, more frequent evaluations or reinterventions were performed. Postoperative imaging was primarily performed with CT, but could be replaced with ultrasound (US) imaging in infrarenal aneurysms with no clinical sign

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of reinfection. In case of suspected graft infection, 18-fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT) was performed.

Survival data were obtained from the Swedish national population registry in July 2008. Survival analysis was performed according to Kaplan-Meier method by using SPSS 16 software (SPSS, Chicago, Ill).

RESULTS

Patient characteristics. We identified 12 patients treated for MAA. One patient treated with open repair was excluded, and 11 patients (8 men) with 13 MAAs treated endovascularly were the basis of this report. Mean age was 70 years (range, 50-80 years). Five patients had predisposing factors affecting the immune system, including immunosuppressive therapy (n = 2), diabetes (n = 2), and renal failure requiring dialysis (n = 1).

Clinical presentation, laboratory, and radiologic findings. All patients had pain and elevated levels of inflammatory markers (leukocytosis or C-reactive protein, or both) as well as typical radiologic findings for MAA at presentation, including saccular aneurysm in 10, periaortic inflammation in 3, rapid expansion in 2, periaortic soft tissue mass in 2, and eccentric aneurysm with narrow neck in 1. Nine had fever, and six had miscellaneous other symptoms, including weight loss, diarrhea, recurrens paresis, hematemesis, dysphagia, and nausea. Seven patients had a concurrent infection comprising abscess in the iliopsoas muscle in 2, tuberculosis in 2, osteitis/spondylitis in 1, soft tissue infection in 1, and enteritis in 1. Positive blood-cultures in six patients showed *Salmonella* species in 2, *Mycobacterium malmoense* in 2, *Staphylococcus aureus* in 1, and *Bacillus cereus* in 1 (Table). Five patients had negative cultures, of whom two were treated with broad-spectrum antibiotics before culture. One patient with antibiotic treatment before culture had a recent history of *Salmonella*-positive gastroenteritis, and one patient without prior antibiotic therapy had a coexisting soft-tissue infection.

Location and rupture. The aneurysms were localized in the aortic arch in 1 patient, descending thoracic aorta in 4, suprarenal abdominal aorta in 3, and infrarenal abdominal aorta in 5 (Table 1). One patient had two separate mycotic aneurysms in the descending thoracic aorta and infrarenal abdominal aorta at the time of diagnosis. In one patient, a suprarenal mycotic aneurysm developed 2.5 years after the treatment of an infrarenal MAA. Five aneurysms presented with rupture, which was contained in three, and eight were without signs of rupture (Fig 1).

Surgical treatment. A tubular TAG stent graft (W. L. Gore & Assoc, Flagstaff, Ariz) was used in the treatment of six aneurysms (Fig 2), of which one was combined with an extra-anatomic deviation of the left subclavian and carotid arteries comprising a carotid–carotid crossover and a left carotid–subclavian bypass. Seven MAAs were treated with a bifurcated Excluder (W. L. Gore & Associates) or Zenith (Cook Inc, Bloomington, Ind) stent graft. One of these required an extra-anatomic deviation of the visceral arteries, which was done in a one-step procedure with a transperitoneal approach, using a Dacron prosthetic graft with inflow from the infrarenal aorta (Table 1). Two patients with a concurrent abscess in the iliopsoas muscle were treated with drainage, and one patient with a soft tissue infection in the first toe required an amputation.

Medical treatment. All patients were given antibiotics preoperatively and postoperatively, initially with broad-spectrum antibiotics intravenously and later, when discharged from the hospital, oral treatment guided by culture results, when available. Antibiotic therapy was administered after consultation with infectious disease specialists. Patients with negative cultures received broad-spectrum antibiotic therapy based on clinical suspicion of infective agent. Seven patients received antibiotic therapy throughout the follow-up period or until death. Three patients stopped antibiotic therapy at 2, 6, and 18 months. A new MAA developed in one of these patients, who ultimately died because of complications of treatment. The other two had raised levels of inflammatory markers during follow-up but were asymptomatic.

Follow-up and outcome. Mean follow-up (time from repair until data was retrieved in July 2008) among survivors was 27 months (range, 13-47 months). No patient was lost to follow-up. No evidence of late prosthetic graft infection was seen on postoperative CT (performed in all patients) or PET-CT (performed in two patients). According to Kaplan-Meier analysis, 1-month survival was 91%, and 1-year survival was 73% (Fig 3).

Outcome for all patients is presented in the Table 1. One death occurred ≤30 days postoperatively: a patient treated with a tubular stent graft for an MAA in the descending thoracic aorta had a fatal bleeding from an aortoesophageal fistula on day 30. Two additional patients died ≤1 year. One patient with end-stage renal disease and active tuberculosis who was treated with a tubular stent graft for an MAA in the descending thoracic aorta suddenly died at 3 months of an unknown cause, and one patient treated with a bifurcated stent graft for a suprarenal MAA died of sepsis at 8 months. At 2.5 years after a successful endovascular repair of an infrarenal MAA and after 18 months of antibiotic treatment, a new mycotic aneurysm developed in the suprarenal aorta in one patient. This was also treated endovascularly, but the patient died 14 days after this second intervention because of occlusion of the superior mesenteric artery due to stent migration that caused intestinal ischemia. The last three patients mentioned were all immunosuppressed because of steroid treatment for polymyalgia rheumatica, immunosuppressive treatment after renal transplantation, or renal failure requiring dialysis, and they all had a poor outcome (Table).

Three of the six culture-positive patients died: one each of new MAA with postoperative stent migration, aortoesophageal fistula, and sepsis; two had complications with postoperative sepsis; and one was treated without complications. One of the culture-negative patients died of an unknown cause, two had raised levels of inflammatory markers, and two were treated without complications.

Table. Patient characteristics, treatments, and outcomes

Age	*Comorbidity*	*Aneurysm localization*	*Culture*	*Rupture*	*Treatment (year)*	*Follow-up time (months)*	*Outcome*
77	Steroid treated polymyalgia rheumatica	Infrarenal aorta and later suprarenal aorta	*Mycobacteria*	...	Bifurcated stent graft (2003) and tubular stent graft with coverage of tr. coeliacus (2006)	24 0.5	Dead (intestinal ischemia due to stent migration with coverage of SMA)
50	Renal failure with dialysis, active tuberculosis	Descending thoracic aorta	...	...	Tubular stent graft (2003)	3	Dead (cause unknown)
77	CABG 2 years earlier, surgically and BCG treated bladder cancer with post-op severe recurrent sepsis 1 month earlier	Infrarenal aorta	*B. cereus*	CR	Bifurcated stent graft (2004)	47	Uncomplicated
74	Hypertension	Infrarenal aorta and descending thoracic aorta	...	...	Bifurcated and tubular stent graft (2004)	46	Uncomplicated
62	Type I diabetes since 40 years	Infrarenal aorta	...	R	Bifurcated stent graft (2005)	37	Elevated inflammatory markers, no vascular complications
80	...	Descending thoracic aorta	*Staphylococci*	CR	Tubular stent graft (2006)	1	Dead (aortoesophageal fistula)
77	Kidney transplantation immunosuppressive drugs for 9 years, tuberculosis	Suprarenal aorta	*Mycobacteria*	...	Bifurcated stent graft with coverage of the native renal arteries (2006)	8	Dead (sepsis)
75	Stroke, CABG 1 year earlier	Infrarenal aorta	...	CR	Bifurcated stent graft (2007)	18	Elevated inflammatory markers, no vascular complications
70	...	Descending thoracic aorta	...	R	Tubular stent graft (2007)	16	Uncomplicated
68	Popliteal aneurysm operated on 2 years earlier	Suprarenal aorta	*Salmonella*	...	Bifurcated stent graft with extra-anatomic deviation of the renal arteries, SMA and tr. coeliacus (2007)	15	Recurrent sepsis, no vascular complications
70	Hypertension, type II diabetes. An infected aortic arch aneurysm treated with open repair (patch) 3 months before endovascular treatment	Aortic arch	*Salmonella*	...	Tubular stent graft with extra-anatomic deviation of the left subclavian and carotid arteries (2007)	13	Recurrent sepsis, no vascular complications

CABG, Coronary artery bypass grafting; *BCG,* Bacille Calmette-Guérin; *CR,* contained rupture; *R,* rupture; *SMA,* superior mesenteric artery; *Tr. coeliacus,* truncus coeliacus.

Autopsy was performed in two of the four patients with fatal outcome, showing the cause of death was intestinal ischemia and aortoesophageal fistula. Postmortem tests for bacterial colonization of the endografts were not performed in these patients. Postmortem examinations were not done in one patient with unknown cause of death because of cultural reasons or in the patient who died in a clinically evident sepsis.

Fig 1. A and B, Preoperative computed tomography angiography of a patient with a ruptured mycotic aneurysm in the descending thoracic aorta.

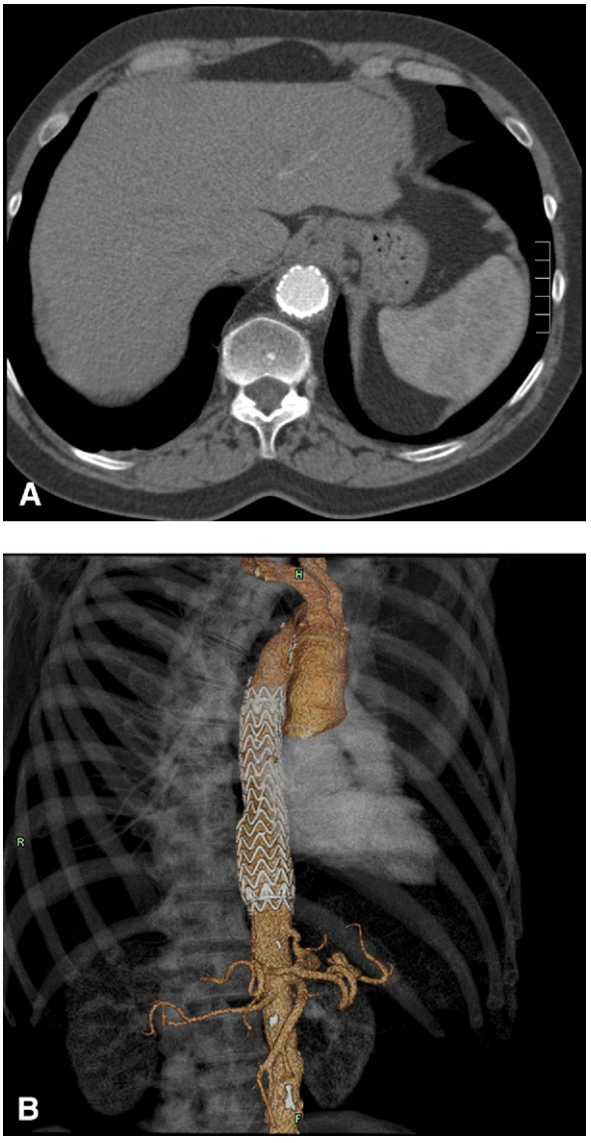

Fig 2. A, Postoperative computed tomography angiography and **(B)** three-dimensional reconstruction after endovascular repair of a ruptured mycotic aneurysm in the descending thoracic aorta. Same patient as Fig 1.

DISCUSSION

A MAA is a major vascular surgical challenge. Because of the high mortality and morbidity associated with major surgery in these diseased patients, minimally invasive endovascular treatment may be a possible therapeutic alternative, especially in high-surgical-risk patients. Owing to the rarity and variable nature of MAAs, a true comparison of open and endovascular treatment strategies is difficult, and the evidence for new treatment strategies will so far have to rely on case series with adequate follow-up. A systematic review published in 2008 by Razavi and Razavi[9] identified 52 reports with a total of 91 patients treated endovascularly

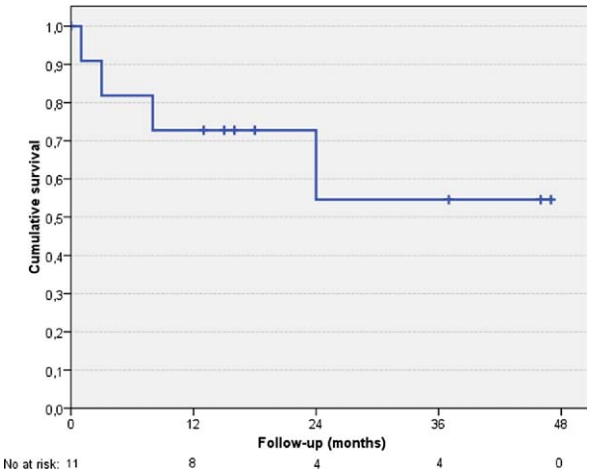

Fig 3. Kaplan-Meier survival plot of 11 patients with mycotic aortic aneurysms treated endovascularly.

for mycotic aneurysms, of which 70 aneurysms were located in the aorta. The largest case series consisted of nine patients with 12 aneurysms. Thus, despite small numbers, to our knowledge the current report is the largest case series to date of endovascular repair of MAA with midterm follow-up.

The definition of an MAA as an aneurysm with proven bacterial infection in the aortic wall creates an inherent limitation in studies of this disease, especially when treated endovascularly, where bacterial culture from the aortic wall cannot be obtained without risk. In this study, as well as in most previous reports,[3,10,11] patients were included based on a clinical diagnosis of MAA, supported by clinical presentation, results of hematologic tests and culture, and CT findings. Anaerobic cultures are difficult to obtain, and these patients often received early broad-spectrum antibiotics, which may explain the 55% rate of positive cultures (6 of 11) in the present report. A positive culture from the aneurysm sac is obtained in 50% to 75% of the cases after open repair of MAA,[3,4,12] and the rate of positive blood cultures in the current study conforms to previous results.

In the present report, three of four patients who died had a positive blood culture at presentation. The correlation between outcome, positive blood culture, and infectious agent are contradictory in the literature.[5,12] On one hand, patients with positive blood cultures may have a more aggressive infection associated with a poor prognosis; on the other hand, a positive culture enables a more precise antibiotic therapy associated with a favorable outcome. Results of routine culture of the abdominal aortic aneurysm wall during surgery of clinically noninfected patients may be positive in 14% to 37%,[13,14] adding to the complexity of this issue.

The 30-day survival in this study of 91% is comparable with the 90% result from a recent systematic review by Kan et al,[7] but the 12-month survival rate of 73% in our study was somewhat lower than the 81% they reported. A review based on several case reports may, however, be subject to publication bias resulting in a falsely high survival rate.

MAA can be treated with open repair and in situ or extra-anatomic bypass with excellent short-term and long-term outcome at specialized high-volume centers.[15] Most reports, however, indicate a short-term mortality >20%,[3, 4,16,17] with significant short-term and long-term morbidity related to the operation.[4,16] In a large series of 43 surgically treated MAAs at Mayo Clinic, survival was 82% at 1 year and 50% at 5 years, with significant surgical morbidity.[6] One study reported a perioperative mortality of 36%,[3] and another reported a 12-month mortality of 30% after open repair for MAA.[5] Thus, although short-term outcome was better after EVAR in this series compared with historical reports on patients undergoing open repair, 1-year survival was not. This decrease in survival during the first postoperative year after endovascular MAA repair in our study could indicate a crossover of survival curves. It is, however, difficult to compare results between different case series of MAA due to selection bias, differences in case–mix, and low number of cases in each series.

The four patients in this study who died all had aneurysms in difficult locations: two were in the suprarenal aorta and two were in the descending thoracic aorta. A minimally invasive approach in these patients was particularly appealing because the perioperative mortality after open repair of suprarenal and thoracic MAAs has been much higher than with infrarenal involvement.[18] No deaths occurred among those treated for an infrarenal MAA in the present report.

Only one patient with MAA was treated with open repair at this center during the study period. At 61 years old, this patient was relatively young, had a relatively low level of comorbidities, multiple suprarenal and infrarenal aneurysms, presented with rupture, and was not a candidate for EVAR. For the 11 patients included in this study, open repair was not regarded as suitable due to complicated anatomy or patient comorbidity and fragility. This potentially affects the comparability of the outcome of this study with historic cohorts of open repair patients.

EVAR has been suggested as a bridge to definitive open repair in treatment of MAA,[19] but this option has not yet been used in any patient in this series. The patients were either doing too well to justify a major open procedure, or they were so fragile with complex anatomy that such an operation was considered too risky. Open repair is preferable in younger patients or in those with continued septic manifestations who are considered fit for surgery. Considering the poor outcome among immunosuppressed patients, it is possible that EVAR should be regarded as a palliative measure or bridge to open repair in this specific patient group. However, it is evident that the presence of a stent graft could complicate a later open repair in many ways, and primary open repair is preferable for patients considered eligible for this therapy.

Kan et al[7] concluded that aneurysm rupture and perioperative fever are the only significant predictors of persistent infection after EVAR of an MAA and such patients should therefore be considered for later open repair. In our experience, however, patients with MAA are often old, with

severe and often multiple comorbidities, and therefore seldom are considered suitable for later radical surgery. Furthermore, until now no radiologic sign of prosthetic graft infection has been observed among the patients treated.

Most patients in this study had long-term antibiotic treatment postoperatively. Still, there was a high incidence of recurrent sepsis (three patients, one with fatal outcome), and a second mycotic aneurysm developed in one patient 1 year after termination of 18 months of antibiotic therapy for the first MAA. This raises the question whether the stent graft might have caused the recurrence. It is notable, however, that the patient was well for 2.5 years while receiving steroid treatment and the second aneurysm developed after termination of antibiotic therapy. The duration and choice of antibiotic therapy, and the potential need for lifelong treatment, is an important matter for further debate, requiring longer follow-up data in a larger group of patients.

CONCLUSION

In this single-center case series, endovascular repair of MAA had acceptable rates of perioperative mortality and midterm survival. Recurrent sepsis as well as late relapse with a second MAA occurred, indicating the need of long-term antibiotic therapy and follow-up, as well as the possible need for a secondary open repair in selected cases. Further research is warranted to evaluate long-term outcome.

AUTHOR CONTRIBUTIONS

Conception and design: KS, MB, AW
Analysis and interpretation: KS, KM, MB, RN, AW
Data collection: KS, KM, AW
Writing the article: KS, KM, AW
Critical revision of the article: MB, RN
Final approval of the article: KS, KM, MB, RN, AW
Statistical analysis: KS, KM, AW
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Overall responsibility: AW

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